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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/206,040	Applicant(s) Byrum et al.
	Examiner Scott D. Priebe, Ph.D.	Group Art Unit 1632

☒ Responsive to communication(s) filed on *Jul 6, 1999* .

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-3* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-3* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *12*

☒ Interview Summary, PTO-413, Paper #11

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

The amendment and response filed July 6, 1999 (Paper No. 13) has been entered. Claim 4 has been cancelled. Claims 1-3 have been amended.

Claim Rejections - 35 USC § 101 & 112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 remain rejected under 35 U.S.C. 101 for the reasons of record set forth in the Office action of April 20, 1999 (Paper No. 10) because the claimed invention is not supported by either a specific asserted utility or a well established utility.

Claims 1-3 remain rejected under 35 U.S.C. 112, first paragraph for the reasons of record set forth in the Office action of April 20, 1999 (Paper No. 10) because:

1) the claimed invention is not supported by either a specific asserted utility or a well established utility, one skilled in the art clearly would not know how to use the claimed invention; and

2) claims 1 and 3 contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention as directed to nucleic acid molecules comprising or consisting essentially of the EST of SEQ ID NO: 1 and additional nucleotide sequences linked to the EST for use in the disclosed utilities.

Applicant's arguments filed July 6, 1999 (Paper No. 13), referred to hereafter as the Response, have been fully considered but they are not persuasive.

Rejection under 35 USC § 101 & 112 because the claimed invention is not supported by either a specific asserted utility or a well established utility. On page 4 of the Response, it is asserted that ESTs inherently have utility because they relate to mRNA molecules known to function *in vivo*. However, this assertion is not supported by any showing of evidence. Also, this assertion raises two issues: a) whether merely knowing that an uncharacterized gene has *in vivo* function is sufficient to confer utility; and b) whether isolation of a cDNA (EST) proves that the hypothetical template for the cDNA relates to a functional mRNA *in vivo.*

On the first issue, the specification does not disclose a specific asserted utility based merely on knowing that a hypothetical mRNA, relating to the EST, is functional *in vivo*, nor has Applicant explained how this knowledge would lead the skilled artisan to a readily apparent utility. At best, knowledge that a product has an unknown or uncharacterized function provides motivation to further characterize the product, i.e. an invitation to further experimentation on the

claimed invention. A product whose sole utility is in research on itself is not eligible for patent protection. See *In re Kirk*, 376 F.2d 936, 153 USPQ 48 (CCPA 1967).

On the second issue, merely because one is able to obtain a cDNA made from a presumed purified preparation of cellular RNA, including mRNA, it cannot be concluded that such cDNA corresponds to an mRNA that would be translated to produce a biologically active product; particularly when the cDNA is arbitrarily selected from a library of heterogeneous cDNA clones. First, any specific cDNA or EST, especially from a heterogeneous library, may be an artifact of the method used to make it. Second, not all mRNAs produced in a given higher eukaryote are functional *in vivo*.

On the first point, as disclosed in the specification polymerase chain reaction (PCR) was used to make a heterogeneous cDNA mixture, which mixture was subsequently cloned to make a cDNA library. One particular cDNA clone was chosen arbitrarily to then determine the sequence of an EST, later set forth as SEQ ID NO: 1 (specification pages 67-68). The thermostable DNA polymerases commonly used in PCR are known to be error prone, such that at the end of PCR a significant fraction of the final nucleic acid molecules contain misincorporated nucleotides (See page 4 of Hayashi, "Manipulation of DNA by PCR", in The Polymerase Chain Reaction, Mullis et al. (eds.), Birkhauser: Boston, pp. 3-13, 1994). Also, amplification of DNA by PCR is known to be exquisitely sensitive to contamination, by genomic DNA or foreign nucleic acid molecules for example (See Kitchin et al., "Avoidance of false positives", Nature 344: 201, 1990, and pages S188-S190 of Roux, "Optimization and troubleshooting in PCR", PCR Meth. Appl. 4 (5): S185-

S194, 1994). Also, PCR is known to generate chimeric DNA molecules if related sequences are present in a biological sample (see Shuldiner et al., "Hybrid DNA artifact from PCR of closely related target sequences", Nucleic Acids Res. 17 (11): 4409, 1989). Kurata et al. (Nature Genetics 8: 365-372, 1994; Ref. AS2 filed 3/4/99) evaluated 2,950 cloned cDNA sequences from *Oryza sativa* (rice) and found that over two-thirds of the cDNAs hybridized to multiple genomic fragments. Kurata et al. concluded that this two-thirds of cDNA sequences were derived from sequences repeated in the genome (Kurata et al., page 366, col. 1). Shi et al. (J. Hered. 87: 308-313, 1996) disclose that nearly 60% of soybean genomic DNA may be repetitive and such repetitive DNAs are difficult to map genetically (page 312, col. 3). Thus, it is more likely than not that the disclosed EST, SEQ ID NO: 1, is derived from a repeated sequence, and there is a significant chance that it is a chimera of related sequences. In choosing PCR reaction conditions for a given application, the artisan must balance the conflicting goals of specificity of priming, fidelity or accuracy of replication and efficiency of product formation (product yield) to produce a desired result (see page 37 of Cha et al., "Specificity, efficiency, and fidelity of PCR", in PCR Primer: A Laboratory Manual, Dieffenbach et al. (eds.), Cold Spring Harbor Laboratory Press: Cold Spring Harbor, NY, pp. 37-51, 1995). The specification provides no information regarding the PCR conditions used or controls to ensure that the disclosed EST (SEQ ID NO: 1) faithfully corresponds to any naturally occurring soybean nucleic acid. Therefore, when the technical problems of using PCR to make cDNAs is taken as a whole in the absence of disclosed controls in

the specification, it is more likely than not that the EST disclosed as SEQ ID NO: 1 is an artifact that does not correspond sufficiently to a naturally occurring soybean nucleic acid.

Second, there exist in higher eukaryotes, including plants, genes which do not encode an active polypeptide product. Such genes collectively are called pseudogenes. Some pseudogenes are not transcribed, i.e. no mRNA would be produced from such pseudogenes. Other pseudogenes are transcribed, and either are not translated or are translated to produce a polypeptide with no biological function. Transcribed pseudogenes are not to be confused with polypeptides produced upon expression of a mutant copy of a normally functional gene. For examples of known transcribed pseudogenes in plants, see Brandt et al. (Curr. Genet. 24 (4): 330-336, Oct. 1993), Quinones et al. (Plant Mol. Biol. 31 (4): 937-943, Jul. 1996), Barakate et al. (J. Mol. Biol. 229 (3): 797-801, Feb. 5, 1993), and Mundel et al. (Curr. Genet. 30 (5): 455-60, Nov. 1996). The phenomenon of transcribed pseudogenes has not been widely studied, and no estimates of the percentage of transcribed genes in various organisms which are transcribed pseudogenes are available. Thus, it is not true that an EST definitely corresponds to a functional gene or gene product in the absence of further characterization, because the EST may correspond to a pseudogene. Therefore, the asserted basis for utility that an EST relates to an mRNA functional *in vivo* is illusory.

It is asserted that ESTs have demonstrated usefulness by commercial success in spawning a multi-million dollar growth industry. As evidence, documents were provided in the information disclosure statement of July 6, 1999 showing that some biotechnology companies derive

significant revenue from EST databases, as summarized in the footnote on page 4 of the response. However, the instant claims are drawn to nucleic acid molecules, not EST databases - which are collections of information. While biotechnology companies are able to generate revenue through the sale or lease of EST information such evidence is not dispositive to the issue at hand, which is the utility of the claimed polynucleotides, because commercial success is impacted by a variety of factors, such as advertising and marketing, which fail to necessarily relate to specific and substantial use in a readily available form. In a related issue, it is asserted that the claimed nucleic acid molecules have utility as a standard for sequence comparison to other nucleic acid molecules (page 10 of Response), citing Examiner's use of the sequence (SEQ ID NO: 1) to identify Shen et al. cited in the rejection under 35 USC 102. A prior art search does not use the claimed nucleic acid *per se*. Instead, it is based upon the chemical formula (SEQ ID NO: 1) for that part of the claimed nucleic acid molecules disclosed as SEQ ID NO: 1. Thus a prior art search uses information, and the claims are not drawn or directed to information, which is subject matter not eligible for patent protection.

Beginning on page 5 of the Response, it is argued that no factual basis was provided that the only readily apparent immediate utilities constituted research on the claimed product, which is a non-statutory utility. However, such factual bases were provided in the analysis presented in Paper No. 10, and were founded upon review of the instant specification. To reiterate, the specification does not provide any characteristics of a claimed nucleic acid molecule comprising the disclosed EST, that would allow it to be used to provide substantial *immediate* benefit to the

public. The only characteristic provided is a single nucleotide sequence. One cannot determine from the disclosed nucleotide sequence alone the corresponding map location; presence or absence of physically-linked sequence polymorphisms; the identity of physically-linked sequence polymorphisms, if indeed present; the size or nucleotide sequence of the complete cDNA or mRNA or gene; the size, amino acid sequence, or biochemical or biological function of any polypeptide encoded by a corresponding gene, mRNA or cDNA; identity of any specific plant tissue expressing the corresponding mRNA; normal levels of the corresponding mRNA in such plant tissue; or the identity of naturally occurring mutations in the corresponding gene. That the specification does not provide any such further characterization of the EST is fact. That the practitioner would therefore be required to engage in undue experimental activity in order to determine such characteristics, which are necessary for using the claimed EST in the disclosed utilities, is therefore also fact. Generalized utilities lack the specific correspondence between the asserted utility and the claimed subject matter required by the statute. As a basis for claims to nucleic acids, this application provides SEQ ID NO: 1, an expressed sequence tag (EST) derived from soybean plant nucleic acid, and asserts that a practitioner could find out where the EST is located in the soybean plant genome, or discover other putative compounds, such as a gene, complete mRNA or protein, that might be related to Applicant's EST. Applicant's assertions regarding the claimed nucleic acids are analogous to the assertions regarding certain steroid compounds in the case *In re Kirk*, 376 F.2d 936, 153 USPQ 48 (CCPA 1967). In that case, "the

nebulous expressions 'biological activity' or 'biological properties'" did not provide a specific and substantial utility that satisfies the statute. 376 F.2d at 941, 153 USPQ at 52.

On page 6 of the Response, it is asserted that the asserted utilities "arise because of the simple fact that the recited sequence corresponds to a mRNA molecule that has some function in the cell because it is a coding sequence". It is further asserted that this simple fact "alone makes the recited sequence immediately useful as a tool in commercial and experimental activities". However, no explanation is given as to how this "simple fact" demonstrates utility. As discussed above this "simple fact" is neither simple nor a fact, but is an assumption or hypothesis. The specification provides no evidence in support of the assumption or hypothesis. There is no evidence that any part of the disclosed EST is polypeptide coding sequence *per se*, or that any mRNA to which it may correspond encodes a biologically relevant polypeptide. Further, the specification fails to identify any hypothetical polypeptide in terms of a putative amino acid sequence, and biochemical or biological function. Therefore, the specification fails to present any evidence for the provision of a useful nucleic acid molecule.

Applicant argues that the EST has utility as a probe for identifying the presence or absence of polymorphisms, and if present, for identifying such putative polymorphisms (pages 6-7). If applicant had found and disclosed that the EST could be used to detect specific sequence polymorphisms between different soybean isolates and if the identity of the polymorphisms had been disclosed, then 35 USC 101 might have been satisfied. However, the fact remains that the specification does not reveal any such polymorphisms nor evidence that any such polymorphisms

could be identified using the EST. Applicants' admission on the record that the initial use of the EST in such a utility is to first determine "the presence or absence of polymorphisms" is a tacit admission that the initial utility is "use testing". If such a use failed to reveal the presence of polymorphisms, then the EST could not be used for identifying polymorphisms or any subsequent utility that relied upon the detection of such polymorphisms; the claimed EST would be useless for the utility of identifying polymorphisms or any subsequent utility requiring the detection of polymorphisms. Thus, whether the specification discloses that polymorphisms can be detected is far from irrelevant, as asserted by Applicants. It is the crux of the issue. The court noted in *In re Kirk*, 376 F.2d 936, 153 USPQ 48, 54 (CCPA 1967) that the argument that "one skilled in the art would know "how to use" the compounds to find out in the first instance whether the compounds *are - or are not - in fact* useful or possess useful properties, and to ascertain what those properties are", is evidence that in fact the requirements of 35 USC 101, and therefore 35 USC 112, 1st para., have not been satisfied. Applicant argues that the mapping function is determined by the sequence disclosed for the EST, and that this would distinguish it from other ESTs (page 11). While true, no mapping information has been provided for the disclosed EST. In the absence of such information this argument represents an invitation to experiment to find a use for what is claimed. For example, one would not be aware of the chromosome or region of a chromosome for which the disclosed EST would be useful as a mapping marker. One must first determine the specific use *vis a vis* the map location detected by the EST before determining or developing a real world use for the claimed nucleic acid molecules.

Applicant asserts that the EST has utility as a probe for determining location on a physical map and to locate the position of the gene on the physical map or genetic map. This argument is supported by reference to the specification where it is stated that physical and genetic maps can be used to characterize or isolate genes corresponding to desirable traits or to screen for desirable traits (page 35, lines 5-7; page 35, lines 17-19). However, the specification provides no information on either the physical map location or genetic map location (or for the latter, fails to provide the identity of polymorphisms by which the genetic map location could be determined). In addition, the specification does not reveal whether the disclosed EST would hybridize to a single location in the soybean genome. The results of Kurata et al. and Shi et al. discussed above suggest that the genomes of plants, and soybean in particular, include a high number of repeated sequences. If the disclosed EST represents or includes repeated sequences and therefore corresponds to multiple genomic locations, it is unclear how it could be used for either genetic or physical mapping. Therefore, it is unclear how the claimed nucleic acid molecules comprising or consisting of the disclosed EST can have these utilities until the copy number and the physical or genetic map locations are determined. Therefore, using the claimed nucleic acid molecules for mapping would first require determining whether the EST corresponded to a single genomic location and, if so, mapping the chromosomal location corresponding to the EST on a physical or genetic map. Consequently, the only *immediate* utility is research on characterizing the claimed nucleic acid molecules, which is use testing and, therefore, non-statutory. Furthermore, it is unclear which genes are to be mapped; the hypothetical gene corresponding to the EST or a

hypothetical gene corresponding to a desirable trait linked to the hypothetical gene corresponding to the EST. With respect to the former, no function either for the putative gene corresponding to the EST or any product expressed from such a gene has been identified. If the gene (or its product) has no known function, knowing its location on a physical or genetic map is at best a scientific curiosity. Also, the specification fails to disclose genes corresponding to desirable traits that are either physically or genetically linked to a gene that might correspond to the EST, and hence the claimed nucleic acid molecules. First, mapping the chromosomal location that might correspond to the EST and then using this information to screen for genes corresponding to desirable traits is nothing more than use testing, i.e. research on identifying a desirable gene whose location can be mapped near to that corresponding to the EST.

It is asserted that the claimed nucleic acids have utility as probes for other molecules or a source of PCR primers to isolate other nucleic acids. The specification has not disclosed any nucleic acid molecule that could be identified using the disclosed EST *vis a vis* the claimed nucleic acid molecule. The Response suggests that a promoter could be identified. Theoretically, if the EST disclosed is a cDNA copy of part of an mRNA present in soybean, then presumably, in the genome there is a promoter region adjacent to the start site of transcription of the mRNA. However, the specification does not disclose any full length mRNA; does not disclose the nucleotide sequence at the beginning of the mRNA or the relative position of the EST within any mRNA species; does not disclose whether the primary transcript contains introns, in which case it could be significantly larger than the mature mRNA; and does not disclose the position of the

EST in the primary transcript and thus the transcribed DNA of the gene. There is no indication of the physical distance separating this hypothetical promoter and sequences in a gene that might correspond to the disclosed EST sequence. Such a distance could be quite large. Furthermore, there is no disclosure of any identifying features of such a promoter. For example, is the promoter regulated and if so by what mechanism is it regulated. Therefore, at best the claimed nucleic acid molecule can be used to initiate a "chromosome walk" cloning procedure on an unidentified chromosome, which, if done in the proper direction, may eventually lead to cloning of a promoter in whole or in pieces; if not the promoter of a gene possibly corresponding to the disclosed EST, then a promoter on the same chromosome. However, the specification provides no information that would allow one to determine when the hypothetical promoter has been obtained or how to identify it if it had been obtained. This is not a specific asserted utility because it is only hypothetical. The specification does not identify any specific promoter that could be isolated using the claimed nucleic acid molecule as probe. Any nucleic acid molecule from any plant cell generally serves this purpose, i.e. as the starting point for a chromosome walk in order to clone an uncharacterized promoter, not any specific promoter.

Applicant asserts that the claimed nucleic acid molecules can be used as "antisense inhibitors" (pages 8-9). However, there is no evidence to show that the disclosed EST can be used as an antisense inhibitor. If a full mRNA sequence were known and if one had an assay to measure expression or activity of the polypeptide encoded thereby, then one might potentially be able to identify antisense inhibitors of a gene that might correspond to the disclosed EST.

However, the specification does not disclose any such information. Moreover, the specification does not disclose any utility for inhibiting expression of the gene corresponding to the disclosed EST. In order for one to identify such a utility, one would first have to develop an assay for expression of the gene, then determine the effect that such inhibition would have on a cell or soybean plant or seed, and finally, determine a use for the inhibition.

It is asserted that the claimed nucleic acid molecules can be used to identify proteins that bind to the claimed molecules (page 9). First, the specification does not disclose whether any proteins bind to the claimed nucleic acid molecules or, if so, identify any specific proteins that bind to the claimed nucleic acid molecules. Second, the specification does not disclose what any such hypothetical binding proteins would be used for, or how any knowledge of such binding would be useful even as a scientific curiosity, let alone a specific utility in readily available form.

It is asserted that the claimed nucleic acid molecules can be used to characterize (and presumably isolate) the 'corresponding' mRNA and protein encoded by the mRNA (page 10). However, the specification does not disclose any specific mRNA that could be isolated with the claimed nucleic acid molecule or any protein encoded by such an mRNA. Second, and most important, the specification does not disclose what any such protein would be used for. Again, undue experimentation to determine a use for the protein would be required.

Several putative utilities have been asserted relating to using the claimed nucleic acid molecules as probes to determine whether "a particular mRNA" is present in a sample, and if so how much is present (pages 9 and 10, including reference to microarrays). The specification does

not identify any "particular mRNA" that is detectable using the claimed nucleic acid molecules; does not identify the function of the polypeptide encoded by the "particular mRNA"; does not identify any phenotype or consequence associated with various levels of expression of the "particular mRNA"; and identifies no significant information that would be gleaned from knowing the level of expression of this hypothetical "particular mRNA". Consequently, it is unclear what such a utility would be. One would first be required to determine the preceding characteristics in order to then begin the process of determining a use for the information.

Several of the asserted utilities for the claimed nucleic acid molecule are alleged to reside in the use of the claimed nucleic acid molecule to identify, isolate or make a second product, such as an mRNA, protein or plant cell (transfected with the claimed nucleic acid molecule). In this relationship, the claimed nucleic acid molecule is analogous to an intermediate with the asserted utility of making a second product. In order for a claimed product to have utility by virtue of a second product that can be made using the claimed product, the second product must have utility. See *In re Kirk*, 376 F.2d 936, 153 USPQ 48, 57 (CCPA 1967) which states:

> ... the conclusion is inescapable that, just as the practical utility of the compound produced by a chemical process "is an essential element" in establishing patentability of the process, ..., so the practical utility of the compound, or compounds, produced from a chemical "intermediate", the "starting material" in such a process, is an essential element in establishing patentability of that intermediate.

and

> ... if a process for producing a product of only conjectural use is not itself "useful" within § 101, it cannot be said that the starting materials for such a process, ..., are "useful". It is

> not enough that the specification disclose that the intermediate exists and that it "works", reacts, or can be used to produce some intended product of no known use

This is clearly the case here, where the claimed nucleic acid molecules comprise the disclosed EST, and the EST can be used to isolate further molecules of "no known use". The mRNA and encoded protein have no known utility, nor does the plant cell transfected with the claimed nucleic acid molecule given that the specification fails to disclose any function provided by the disclosed EST itself.

Therefore, the only apparent *immediate* utility for the EST, and therefore the claimed nucleic acid molecules, is further characterization of the EST, which includes characterization of undisclosed products made from or with the claimed nucleic acid molecules. Such *immediate* utility constitutes use testing. There is no "*immediate* benefit to the public", as required to comply with 35 USC 101 (see *Brenner v. Manson*, 383 U.S. 519, 534-535, 148 USPQ 689, 696 (US SupCt., 1966); *Nelson v. Bowler*, 626 F.2d 853, 206 USPQ 881, 883 (CCPA, 1980), *In re Ziegler*, 992 F.2d 1197, 26 USPQ2d 1600 (Fed. Cir. 1993)).

Furthermore, the assertion that a nucleic acid comprising, or consisting essentially of, SEQ ID NO: 1 could be used as a chromosome marker, or in the other proposed ways, is an insubstantial utility in view of the broadly drawn claims, which use open ended transitional terms. As the Supreme Court said in *Brenner v. Manson*, until the invention has been shown to have utility:

> the metes and bounds of that monopoly are not capable of precise delineation. It may engross a vast, unknown, and perhaps unknowable area. Such a patent may confer

> power to block off whole areas of scientific development, without compensating benefit to the public. The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point--where specific benefit exists in currently available form--there is insufficient justification for permitting an applicant to engross what may prove to be a broad field.

383 U.S. 519 at 534-35, 148 USPQ 689 at 695 (1966). The proposed utilities here are insubstantial in comparison to the scope of the claimed subject matter. Thus, the application fails to disclose practical, real world utilities for the claimed nucleic acids comprising or consisting essentially of SEQ ID NO: 1.

On page 11 of the Response it is suggested that the rejection violates PTO Utility guidelines because no evidence had been provided questioning the credibility of the putative utilities disclosed in the specification. However, the courts have required there to be a specific, substantial and credible utility for 35 USC § 101 to be satisfied. See *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (US SupCt., 1966); *Nelson v. Bowler*, 626 F.2d 853, 206 USPQ 881 (CCPA, 1980), *In re Ziegler*, 992 F.2d 1197, 26 USPQ2d 1600 (Fed. Cir. 1993). The presence of only one of these three criteria is insufficient. The USPTO has issued revised utility guidelines consistent with such law [Federal Register, Volume 64, Number 244, December 21, 1999.].

Additional grounds for rejection of claims 1 and 3 under 35 USC § 112, 1st para. for lack of enablement. These additional grounds of rejection were set forth on pages 5-8 of the Office action of April 20, 1999 (Paper No. 10), and concerned a lack of enablement for how to use the full scope of nucleic acid molecules "comprising" or "consisting essentially of" the polynucleotide

set forth as SEQ ID NO: 1. This is a separate issue than that set forth above in regard to the failure of the specification to set forth a specific utility for the claimed invention.

One skilled in the art would know how such molecules could be made. However, the specification fails to provide an enabling disclosure for how to use the claimed nucleic acid molecules as hybridization probe or amplification primer that is commensurate in scope with the claimed nucleic acid molecules. While the disclosure teaches expression vectors comprising the claimed nucleic acid molecules on pages 46-54, the specification fails to disclose any intrinsic biological activity for the disclosed EST (SEQ ID NO: 1), and discloses no biochemical activity other than as probe or primer in a hybridization or amplification reaction. Further, the specification fails to disclose any protein encoded by the disclosed EST present in the claimed nucleic acid molecules or encoded by any mRNA or genomic DNA that might correspond to said EST.

In Applicant's analysis referring to the eight criteria of *In re Wands* (858 F.2d 731, 8 USPQ2d 1400, (Fed. Cir. 1988)), it is asserted that sufficient direction or guidance is provided with respect to labeling the claimed nucleic acid molecules (second criterion). However, this guidance refers to making nucleic acid molecules having altered or modified nucleotide subunits, and thus concerns the nucleic acid molecules set forth in claim 2, wherein the claimed nucleic acid molecule "consists of" SEQ ID NO: 1. Claims 1 and 3 comprise additional nucleic acid sequences since the transitional language "comprising" and "consisting essentially of" is recited. The specification fails to provide adequate guidance on the identity of such additional nucleic acid

sequences in the context of using the nucleic acid molecules of claims 1 and 3 as a probe or primer. It is this lack of guidance that leads to an excessive and undue amount of trial-and-error (or "make-and-test") experimentation (first criterion). It is alleged that Examples 1 and 2 represent adequate working examples (third criterion). These working examples are not adequate because: 1) the plasmids described were made without first knowing that the nucleotide sequence of SEQ ID NO: 1 was present in any of the plasmids present in the cDNA library made; and 2) claims 1 and 3 are not limited to vectors comprising SEQ ID NO: 1, made, for example, by insertion of the EST (SEQ ID NO: 1) into a vector backbone such as pSport.

With respect to the nature of the invention (fourth criterion) it is asserted in the Response that the skilled artisan would use "multiple known methods to obtain the desired result", including "screening to obtain the desired result". Screening would be required where the skilled artisan could not predict (seventh criterion) the performance characteristics of any and all of the essentially infinite nucleic acid molecules (eighth criterion). Whether one skilled in the relevant art is able to make any and all of the claimed nucleic acid molecules or know how to carry out hybridization or amplification using the claimed nucleic acid molecules (sixth criterion) is not at issue. The issue is whether the level of skill in the art and state of the prior art would enable one skilled in the relevant art to predict *a priori* with a reasonable degree of certainty the identity of claimed nucleic acid molecules suitable as a probe or primer or whether the artisan would be required to "make-and-test" the nucleic acid molecules to determine *a posteriori* their suitability as a probe or primer, and whether such empirical "make-and-test" experimental activity is routine

or undue. No evidence has been presented that either the specification or the prior art (fifth criterion) provides the requisite guidance or skill level to allow the artisan to predict which of the essentially infinite nucleic acid molecules claimed (eighth criterion) are suitable for use as a probe or primer. Consequently, "make-and-test" experimentation would be required. Applicants have provided no evidence (nor is Examiner aware of any) supporting the contention that one skilled in the art of nucleic acid hybridization or amplification routinely makes a myriad of nucleic acid molecules comprising a core sequence, such as the EST, and additional arbitrarily or randomly chosen nucleotide sequences, and then screens the myriad of nucleic acid molecules in a hybridization or amplification assay to determine which of the nucleic acid molecules made should be used as probe or primer, respectively, in the reaction. Therefore, the experimentation required to use the claimed nucleic acid molecules in a manner commensurate in scope with claims 1 and 3 is undue, especially since the specification teaches no specific utility for the claimed invention.

With respect to operative or inoperative embodiments of the claimed invention, the Office concedes that a claim may embrace inoperative embodiments and be enabled. However, a claim is only enabled if the specification teaches the skilled artisan how to select operative embodiments and avoid inoperative embodiments without undue experimentation. In the instant case, undue experimentation would be required to select the operative embodiments for the reasons set forth above. As to whether the number of inoperative embodiments would be excessive, since one cannot predict the operative embodiments, the Office cannot estimate the fraction of inoperative embodiments.

Claims 1 and 3 remain rejected under 35 U.S.C. 112, first paragraph, for the reasons of record set forth in the Office action of April 20, 1999 (Paper No. 10), as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant's arguments filed July 6, 1999 (Paper No. 13) have been fully considered but they are not persuasive. Applicant argues that this is a question of "overbreadth". The rejection is not based on breadth alone, but also on the fact that substantial species embraced by the claims are not described. The broadest reasonable interpretation of the claims is that they include full length mRNAs, cDNAs and genes that include SEQ ID NO: 1, the EST. The claims are not limited to short lengths of nucleic acid, nor do they exclude introns, regulatory regions or promoter regions that may be associated with SEQ ID NO: 1 embedded in genomic or other naturally occurring sequences. This interpretation is consistent with the specification. See, e.g., pages 10-15.

Applicant has not characterized any mRNA, cDNA, gene, intron, regulatory region or promoter region with particularity or reasonable clarity such that one skilled in the art would recognize applicant had possession of these inventions embraced by the claims. There is no disclosed correlation between the chemical or physical properties of SEQ ID NO: 1 and the chemical or physical properties of the coding or non-coding elements that SEQ ID NO: 1 would be associated with in the compounds embraced by the claims. Consequently, it is reasonable to

conclude that applicant was not in possession of any such mRNAs, cDNAs and genes at the time the instant application was filed.

Further, claims 1 and 3 embrace an essentially infinite number of nucleic acid molecules, each having the minimum requirement of comprising the nucleotide sequence set forth in SEQ ID NO: 1, but may further comprise any number of additional nucleotides of any sequence or length. In contrast, the specification discloses only SEQ ID NO: 1 and, generically, vectors comprising SEQ ID NO: 1. Such vector sequences are extrinsic to any sequence that might be naturally contiguous with the disclosed EST (SEQ ID NO: 1). The sole exception is the cDNA clone used to determine SEQ ID NO: 1; however, this clone was not deposited and any potential sequences naturally contiguous to SEQ ID NO: 1 are not disclosed. It is noted that in the absence of any information regarding the basic and novel characteristics of the claimed invention, recitation of "consisting essentially of" in claim 3 fails to distinguish the invention of claim 3 from that of claim 1, which recites "comprising".

The issue is whether disclosure of a single nucleotide sequence is an adequate written description of an infinity of nucleic acid molecules comprising it, and in particular the sub-genus embracing mRNAs, cDNAs and genes comprising SEQ ID NO: 1 that one skilled in the art would reasonably consider as being embraced by claims 1 and 3. While the specification provides a written description of claim 2, a nucleic acid molecule consisting of the nucleotide sequence set forth in SEQ ID NO: 1, it does not describe in terms of a precise physical description any and all nucleic acid molecules comprising SEQ ID NO: 1. There is no evidence that applicants were in

possession of the genus of infinite nucleic acid molecules of claims 1 and 3. Consequently, Applicant's description of the claimed compounds is inadequate.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claim 3 under 35 U.S.C. 112, second paragraph, for recitation of "consisting essentially of" in reference to a nucleic acid molecule is withdrawn.

Claims 1-3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-3 each recite "isolated nucleic acid molecule". The term "isolated" has not been defined in the specification. The Response (page 2) indicates that "isolated nucleic acid molecule" was supported in the specification: at page 25, lines 1-19, which passage does not use "isolated"; at page 66, line 25 to page 67, line 6, which passage uses the term "isolation" in the context of DNA and clones, but does not further clarify what is meant by "isolation"; and at page 67, line 25 to page 68, line 7, which passage describes isolation of plasmid DNA comprising an EST from a cell clone containing it in preparation for DNA sequencing. None of these passages indicate the degree to which the claimed nucleic acid molecules is isolated or from what other

constituents it is isolated. In addition, the pertinent art taken as a whole does not provide a recognized definition for "isolated" in the context of polynucleotides.

Originally the claims recited "substantially purified", which is very broadly defined in the specification at page 15, para. 4, as "one or more molecules that is or may be present in a naturally occurring preparation containing that molecule will have been removed or will be present at a lower concentration than that at which it would normally be found". For reasons of record set forth in Paper No. 10 at pages 9-10, this definition was deemed unclear. In view of the very broad and unclear definition of "substantially purified" in the specification and the lack of a definition of "isolated" in the specification or in the pertinent art, the meaning of the term "isolated"cannot be determined. Consequently, the metes and bounds of the claimed nucleic acid molecules is unclear.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 3 remain rejected under 35 U.S.C. 102(b) as being anticipated by Reams for the reasons of record set forth in the Office action of April 20, 1999 (Paper No. 10).

Claims 1 and 3 remain rejected under 35 U.S.C. 102(b) as being anticipated by Choi et al. (Plant Physiol. 101 (2): 699-700, 1993) for the reasons of record set forth in the Office action of April 20, 1999 (Paper No. 10).

Applicant's arguments filed July 6, 1999 (Paper No. 13) have been fully considered but they are not persuasive. Applicants assert that the replacement of "substantially purified" with "isolated" overcomes the rejections of claims 1 and 3 under 35 USC § 102(b). However, as indicated above in the rejection of these claims for recitation of "isolated", the metes and bounds of claims 1 and 3 is unclear. There is no indication in the specification that recitation of the term "isolated" in claims 1 and 3 excludes any embodiments of the invention that read on the prior art cited in these rejections. A reasonable interpretation of "isolated" embraces a total nucleic acid preparation from soybean cells, since the nucleic acid would be isolated from non-nucleic acid compounds, such as proteins and lipids, present in a soybean seed, especially when interpreting "isolated" in light of the description of "substantially purified" in the specification.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Certain papers related to this application may be submitted to Art Unit 1632 by facsimile transmission. The FAX number is (703) 308-4242 or 305-3014. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe whose telephone number is (703) 308-7310. The examiner can normally be reached on Monday through Friday from 8 AM to 4 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jasemine Chambers, can be reached on (703) 308-2035.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Scott D. Priebe

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